

REMARKS

Claims 1-9 are pending and have been amended.

FORMAL DRAWINGS

The Office Action stated, "The drawing(s) filed on 08 January 2004 is/are: objected to by the Examiner." (Office Action, page 1, box 10). Contrary to the assertion of the Office Action, applicants did not submit drawings on January 8, 2004 in connection with the subject application. Nevertheless, applicants submit herewith two sheets of formal drawings for Figures 1 and 2. The formal drawings submitted herewith do not raise an issue of new matter.

IDS ENTITLED TO CONSIDERATION

On May 28, 2004, after the date of the Office Action, applicants submitted a Supplemental Information Disclosure Statement (IDS) to make of record an International Search Report issued in connection with the PCT International Application corresponding to the subject application. The May 28, 2004 Supplemental IDS contained the Statement specified in 37 CFR 1.97(e)(1). Accordingly the Supplemental IDS is entitled to consideration. Applicants respectfully request an initialed copy of the Form PTO-1449 submitted therewith. Claims 1-9 in the pending application correspond to claims 1-5 and 67-70 of the international application.

CLAIMS ARE NOT INDEFINITE

The claims have been rejected under 35 U.S.C. §112, second paragraph. This rejection is respectfully traversed. The Office Action presents three grounds for the rejection, each of which is addressed below.

The first ground of rejection related to the recitation of "A biologically active agent" in the preamble of claims 1 and 2. Although applicants disagree with the basis of the rejection, in order to advance prosecution the preambles of claims 1 and 2 have been amended to recite a "compound" as recommended in the April 8, 2004 Office Action. The dependent claims have been amended to conform to the amendment of claim 2.

Support for the claims as amended may be found, *inter alia*, in the claims as originally filed. Applicants maintain that the amendment does not introduce new matter. The original preamble did not limit the claims. It neither recited essential structure or steps, nor was it necessary to give life, meaning and vitality to the claim, nor did applicants rely on the preamble to distinguish the claimed invention from the prior art. Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc., 289 F.3d 801, 808 (Fed. Cir. 2002).

The second ground of rejection is based on the alleged difficulty in visualizing the claimed compounds. The rejection states:

Claims 1, 2 recite provisos, but do not exactly and definitely spell out the compounds claimed as a novelty. What is excluded in claim 1 is included in claim[2]. Therefore, it is very difficult to visualize the claimed compounds.

Office Action, page 3. Contrary to the above allegation, claims 1 and 2 identify the claimed subject matter distinctly and with particularity in accordance with the requirements of Section 112, second paragraph. Claims 1 and 2 are written in Markush format and contain a chemical structure and values for the variables that appear in that structure. There is no ambiguity as to what is included or excluded by the claims. Section 112, second paragraph, requires no more.

The rejection alleges that the provisos which render claims 1 and 2 non-overlapping make it difficult to visualize the claimed compounds. However the need for effort to

construe the claims is not sufficient to support a rejection for indefiniteness. "Claims need not 'be plain on their face in order to avoid condemnation for indefiniteness; rather what [the CAFC has] asked is that the claims be amenable to construction, however difficult that task may be.'" SmithKline Beecham Corp. v. Apotex Corp., 365, F.3d 1306, 1314, 70 USPQ2d 1737, ____ (Fed. Cir. 2004), quoting Exxon Research & Eng'g Co. v. United States, 265 F.3d 1371, 1375. In this case each of claims 1 and 2 recites a definite chemical structure and is plain on its face to an organic chemist.

The third ground of rejection incorrectly alleges ambiguity in the definition of one of the variables. The rejection stated:

Claims 1, 2 recite X component as: "a group consisting of -NHAc"
What is excluded in the definition of AC[?] The claim[s] read on to AC as
-COCF₃ in addition to -COCH₃ as well.

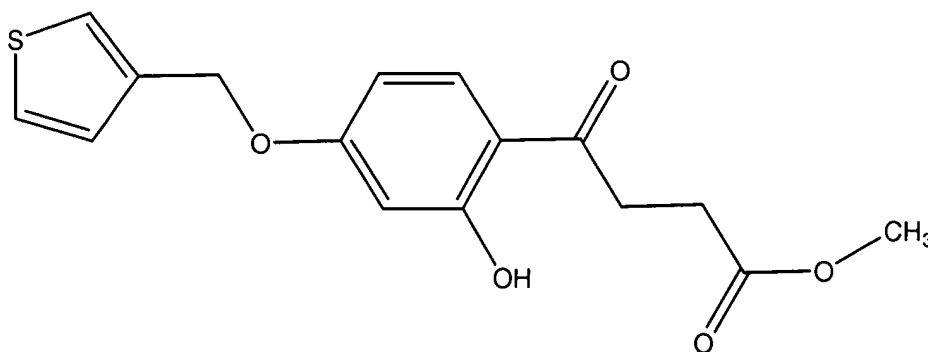
Office Action, page 3. X can be, *inter alia*, -CH₂CH(NHAc)-, but X is not -NHAc as wrongly stated in the rejection. The above-quoted passage from the rejection is also wrong in stating that Ac reads on COCF₃. Applicants direct the attention of the Office to the specification of the subject application which defines Ac as follows: "As used herein 'Ac' refers to the group CH₃C(O)-." (Specification, page 9, line 26).

In view of the amendment and the preceding remarks applicants respectfully maintain that the rejection under Section 112, second paragraph, is improper and should be withdrawn.

INVENTION NONOBVIOUS OVER WO 95/13262

Claims 1-9 have been rejected under 35 U.S.C. 103 as allegedly being obvious over WO 95/13262 (Astles et al.). A copy of the full-length Astles reference is enclosed. This rejection is respectfully traversed.

The rejection is based on the teaching by Astles of CAS RN #170283-05-03; 4-(2-hydroxy-4-(3-thienylmethoxy)-phenyl)-4-oxo-butanoic acid methyl ester, having the following structure:



The rejection acknowledged that “the ref. ‘262 differs from the instant invention by having phenyl ring substituted by a OH group instead of -O-alkyl/H as claimed herein.” (Office Action, paragraph 7).

The rejection alleges that “it would have been obvious . . . to prepare instant compounds by modifying or replacing H of -CH- group of benzene ring with other groups E.g. -OH or -Oalkyl or -O-substituted alkyl or a halogen. . . .” (Office Action, paragraph 8). Even assuming, for the sake of argument, that it would have been obvious to change one of the benzene ring hydrogens to hydroxy, alkyloxy or halogen as asserted in the rejection, such changes would not yield the claimed compounds. The compound resulting from such allegedly obvious changes would be substituted on the benzene ring by two hydroxyl groups, or one hydroxyl group and one alkyloxy group, or one hydroxyl group and one

halogen group. Such allegedly obvious compounds do not read on the pending claims. Accordingly, the rejection is wrong in alleging that such changes are a way “to prepare instant compounds.” (Office Action, paragraph 8). The rejection has not presented any reasoning for finding the claimed invention obvious.

To arrive at a compound that reads on some of the pending claims (claims 1, 2 and 4-6), one would have to change hydroxyl in the reference compound to hydrogen, alkoxy or halogen. Yet the rejection has not even alleged that such a change would have been obvious, and certainly has not presented any reasoning that would justify considering such a change to be obvious. The “obvious to try” approach attempted by the Office Action in support of a different obviousness allegation fails here as well and for the same reasons.

In explaining the reasoning behind a different allegedly obvious change the rejection utilized an improper “obvious to try” approach. The rejection stated that “it would have been obvious to . . . try out the use/utility as a pharmaceutical The motivation stems from the expectation of making compounds having equal or better pharmaceutical” activity. (Office Action, paragraph 8) (underlining added). This “obvious to try” approach is an insufficient basis for an obviousness rejection. A general motivation to search for a compound having desirable properties does not render obvious the specific compound that is ultimately obtained. In re Deuel, 51 F.3d 1552, 1558, 34 USPQ2d 1210, ____ (Fed. Cir. 1995) (“A general motivation to search for some gene that exists does not necessarily make obvious a specifically-defined gene that is subsequently obtained as a result of that search.”)

In addition to the foregoing errors, the rejection minimizes the differences between claims 8 and 9 and the reference compound. The rejection stated that the reference compound “differs from the instant invention by having phenyl ring substituted by a OH group instead of -O-alkyl/H as claimed herein.” (Office Action, paragraph 7). But that is not the only difference. The compound of claim 8 has a pyridinyl group rather than a

thienyl group as in the reference compound. No reasoning based in the prior art or the knowledge available to those of ordinary skill in the art has been given to explain why it would have allegedly been obvious to substitute pyridinyl for thienyl.

The compound of claim 9 has a thienylethoxy group rather than a thienylmethoxy group as in the reference compound. The rejection asserts that "analogous alkyl . . . bridge variations would be structurally obvious." (Office Action, paragraph 9) (citations omitted). That might be enough to establish *prima facie* obviousness if the differing alkyl bridge lengths were the only difference between claim 9 and the reference compound. But that is not the only difference. In the compound of claim 9 the benzene ring is not substituted by hydroxyl as in the reference compound. To arrive at the compound of claim 9 one would have to simultaneously change hydroxyl to hydrogen and change thienylmethoxy to thienylethoxy. The rejection has pointed to no suggestion or motivation based in the prior art or the knowledge available to those of ordinary skill in the art to make such simultaneous modifications. Accordingly, the compound of claim 9 as a whole would not have been *prima facie* obvious over the reference compound.

In view of the foregoing, applicants respectfully submit that the rejection over Astles is improper and should be withdrawn.

INVENTION NONOBVIOUS OVER WO 97/15550 AND KAMEO

Claims 1-9 have been rejected under 35 U.S.C. 103 as allegedly being obvious over WO 97/15550 (Chemical Abstract DN 127:5350) (Varasi, et al.) in view of Kameo, et al. (Chem. Pharm. Bull. 37/5, 1260-7 (1989); Chemical Abstract DN 111:108496). A copy of the full-length version of each of the references is enclosed. This rejection is respectfully traversed.

The rejection is based, in part, on the combination of different elements from four different prior art compounds, two from each of the references (Office Action, paragraphs

11 and 12). Two of the compounds are said to have pharmaceutical activities, that are however different from each other. CAS RN# 190124-67-5 (Varasi) is said to be a kynurenine-3-hydroxylase enzyme inhibitor and to be useful in the treatment of neurodegenerative diseases, unlike CAS RN# 122399-35-3 (Kameo) which is said to have hypolipidemic activity. The other two compounds, CAS RN# 190124-52-8 (Varasi) and CAS RN# 122399-86-4 (Kameo) are utilized in the references as synthetic intermediates and are not disclosed to have any pharmaceutical activity.

Someone, like the PTO or an accused infringer, who has the burden of establishing obviousness “cannot pick and choose among the individual elements of assorted prior art references to recreate the claimed invention.” SmithKline Diagnostics, Inc., v. Helena Laboratories Corp., 859 F.2d 878, 887, 8 USPQ2d 1468, ____ (Fed. Cir. 1988). Even when obviousness is based on the combination of different elements in a single reference, “a rejection cannot be predicated on the mere identification in [the prior art reference] of individual components of claimed limitations.” In re Kotzab, 217 F.3d 1365, 1371, 55 USPQ2d 1313, ____ (Fed. Cir. 2000).

What, according to the rejection, would have been the motivation to combine selected elements from these four prior art compounds to arrive at the claimed compounds? It is “the expectation of making compounds having equal or better pharmaceutical” activity. (Office Action, paragraph 13). But the rejection does not, because it cannot, explain why the combination of individual elements selected from two different compounds with different pharmaceutical activities with individual elements selected from two other compounds that have no known pharmaceutical activity would have been expected to result in a compound with any pharmaceutical activity whatsoever. Moreover, the rejection does not explain how the person of ordinary skill in the art “with no knowledge of the claimed invention” (Kotzab at 1371) would have known the right elements to pick and choose from the four prior art compounds. Without the hindsight provided by applicants’ invention, there would have been no suggestion or motivation to comb

through the prior art, selecting specific elements and combining them in just the right way so as to arrive at the claimed invention.

The rejection is also based on an improper “obvious to try” standard. Thus the Office Action argues that “[i]t would have been obvious . . . to prepare instant compounds . . . and try out the use/utility as a pharmaceutical by using the conventional chemistry knowledge. Office Action, paragraph 13 (underlining added). This “obvious to try” approach is an insufficient basis for an obviousness rejection. A general motivation to search for a compound having desirable properties does not render obvious the specific compound that is ultimately obtained. *In re Deuel*, 51 F.3d 1552, 1558, 34 USPQ2d 1210, ____ (Fed. Cir. 1995) (“A general motivation to search for some gene that exists does not necessarily make obvious a specifically-defined gene that is subsequently obtained as a result of that search.”)

The rejection is also based on the incorrect assertion that one or the other of the references discloses a genus that encompasses the compounds claimed by applicant. Thus the rejection states:

It has been held that a prior art disclosed compounds [sic] is sufficient to render a prima facie case of obviousness as [sic] species falling within a genus. See *In re SUSI*, 440 F 2d 442, 169 USPQ 423, 425 (CCPA 1971), followed by Federal Circuit in *Merck & [Co. v.] Biocraft Laboratories*, 847 F 2d 804, 10 USPQ 2d 1843, 1846 (Fed. Cir. 1989).

Office Action, paragraph 15. Contrary to the implication of the above-quoted passage, the claimed compounds are not encompassed by any genus disclosed by either of the references. The Varasi genus does not contain any heteroaromatic rings, unlike the claimed compounds. The Kameo genres encompassing the reference compounds require that the 4-oxobutanoic acid moiety be substituted by either hydroxyl (Formula VIII on page 1260) or acetylthio (Table I on page 1261). Therefore no teaching of either of the references is related to the claimed invention as genus to species.

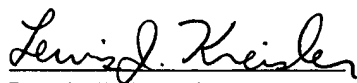
In view of the foregoing, applicants respectfully submit that the rejection over Varasi and Kameo is improper and should be withdrawn.

CONCLUSION

Reconsideration of all objections and rejections is respectfully requested. Applicant believes that the subject application is in condition for allowance and looks forward to a favorable action.

It is believed that no fee is required in connection with the filing of this Amendment. If any fee is required, the Commissioner is hereby authorized to charge the amount of such fee to Deposit Account No. 50-1677.

Respectfully submitted,



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Enclosures: Formal drawings (2 sheets)
WO 95/13262 (Astles et al.)
WO 97/15550 (Varasi, et al.)
Kameo, et al., Chem. Pharm. Bull. 37/5, 1260-7 (1989)